

The FDA's New Reclassification of Rapid Influenza Diagnostic Tests: Are you Prepared?

Presented by:

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September 27, 2017

Learning objectives



Review FDA influenza reclassification requirements and assess impact to currently utilized RIDTs.

Identify the different types of influenza tests available and if they are compliant with the new FDA guidelines.

Understand the pros and cons of each type of influenza testing based on the needs of your laboratory.

Explain the dates until which products not meeting the new guidelines can be sold, as well as how long they can be used for patient testing.

Influenza virus



- RNA viruses
- Belong to the Orthomyxoviridae family
 - Several members of this family
 - Only influenza A and B cause human epidemics
- Have been causing human pandemics for a few hundred years

Influenza A & B in the U.S.



- 5-20% of population is affected each year
- Approximately 36,000 deaths each year with more than 200,000 hospitalizations
 - Ranges from 4,000-50,000 deaths per year
- Most deaths are in elderly
 - But can also occur in healthy individuals (2009 H1N1)

Influenza A vs. B

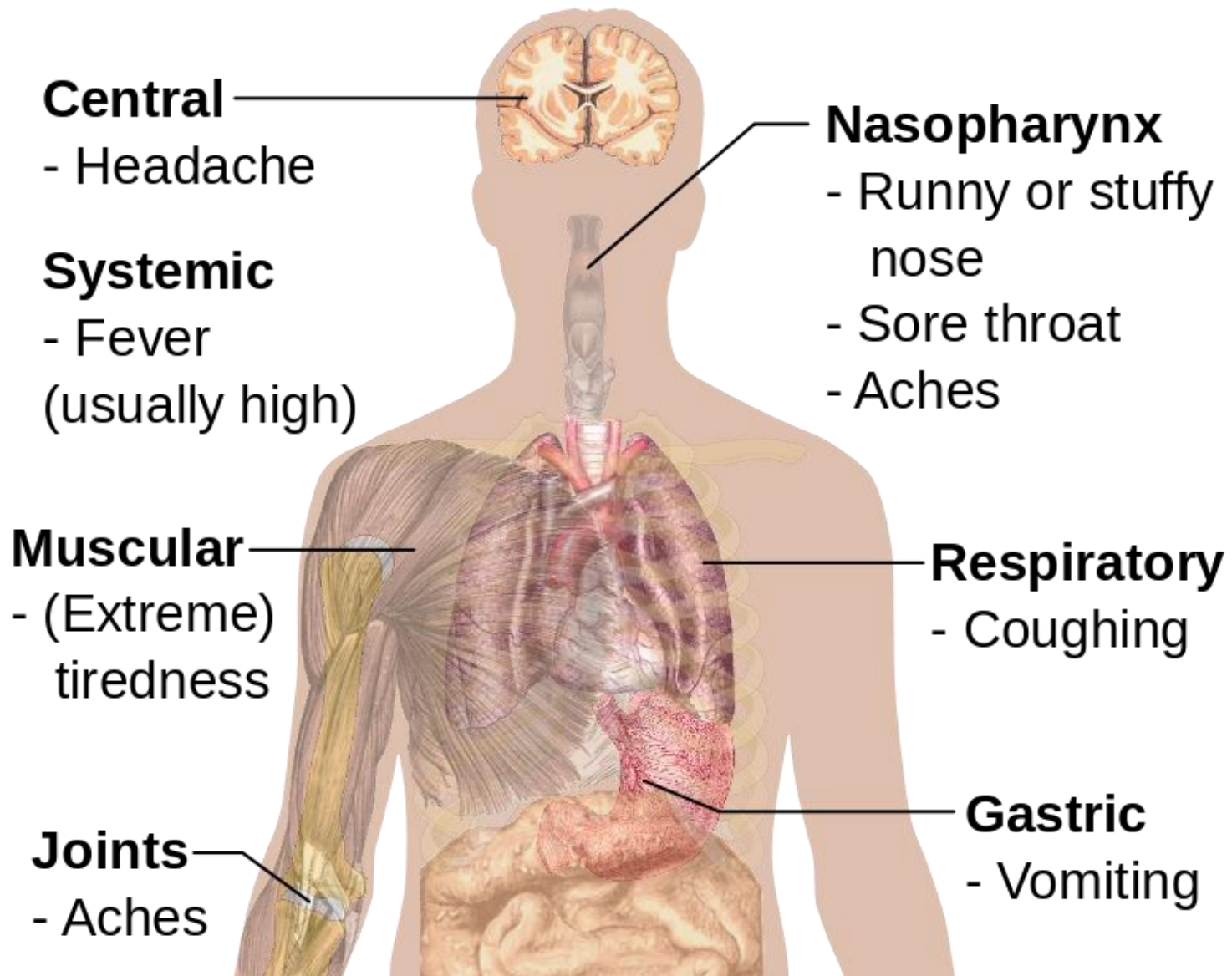
Influenza A

- Can cause disease in a wide variety of animals
- More severe disease than B
- Divided into subtypes based on two surface proteins:
 - Hemagglutinin (H)- ~13 types
 - Allows virus to bind to cells for infection
 - Neuraminidase (N)~ 9 types
 - Allows new viruses to escape from cells

Influenza B

- Causes a milder flu, usually in the spring months
- Broken down into lineages
 - E.g. B/Yamagata, B/Victoria

Symptoms of influenza



Häggström, Mikael (2014). "Medical gallery of Mikael Häggström 2014".

Spread of influenza



- Spread person-to-person
- Droplets spread when coughing, sneezing and talking
 - Can spread about 6 feet away
- Touching contaminated surfaces and then touching nose and/or mouth

Avoiding spread of influenza



- Wash hands!
- Surgical mask
- Vaccination

Remember: You can spread flu one day
before you are symptomatic!

Treatment for influenza



- Most people do not need treatment
- Antiviral drugs can be used for treatment in those at high risk for flu complications
 - Shorten disease duration by 1-2 days
 - Could prevent certain complications
- People at high risk of flu complications:
 - Young children,
 - Adults ≥ 65 years of age
 - Pregnant women
 - Those with certain medical conditions
 - Asthma, diabetes, heart disease, immunosuppressed, etc.

Identification of pneumococcal infection is critical

- ~25% of influenza-related deaths have a secondary bacterial pneumonia¹
- Post-mortem lung tissue from 1918 pandemic showed that most patients also had bacterial infection²
- 1957 pandemic showed that 2/3 of deaths were associated with bacterial pneumonia³

1. Simonsen L. The global impact of influenza on morbidity and mortality. *Vaccine* **1999**; **17**(Suppl 1):S3–10.

2. Hers JF, Masurel N, Mulder J. Bacteriology and histopathology of the respiratory tract and lungs in fatal Asian influenza. *Lancet*. 1958;2:1141–1143. doi: 10.1016/S0140-6736(58)92404-8. [[PubMed](#)] [[Cross Ref](#)]

3. de Roux A, Ewig S, García E, Marcos MA, Mensa J, Lode H, Torres A. Mixed community-acquired pneumonia in hospitalized patients. *Eur Respir J*. 2006;27:795–800. doi: 10.1183/09031936.06.00058605. [[PubMed](#)] [[Cross Ref](#)]

How does the flu virus change?

ANTIGENIC “DRIFT” VS. “SHIFT”

Drift – small genetic changes over time

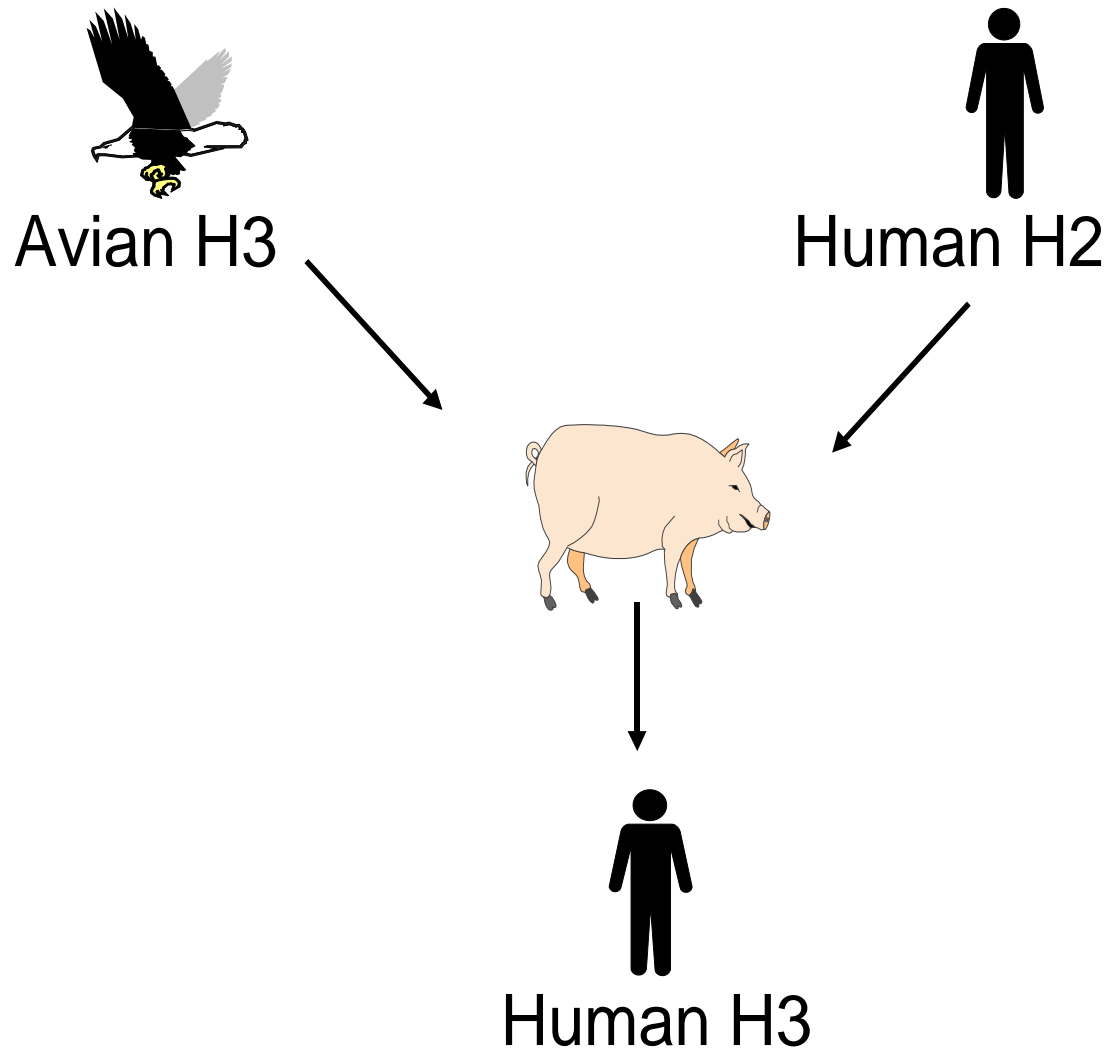
- More typical, yearly change in influenza virus
- Reason why a new vaccine formulation is needed every year, even for the “same” virus

Shift – major change resulting in a new hemagglutinin and/or neuraminidase

- Leads to a new virus to which people’s immune system is naïve
 - Can lead to influenza pandemics
- Occurred in 2009 – Novel H1N1

Changes can and will affect the performance of influenza tests.

How does antigenic shift happen?



This is real.
THIS IS US



SEASON PREMIERE
SEPT 26
TUE 9/8c NBC

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HEALTH

FEB 20 2014, 1:53 PM ET

Flu Killing More Young Adults This Year, CDC Says

Public health officials are encouraging people to get flu shots as the seasonal virus hits young adults hard this year. Justin Sullivan / Getty Images

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Influenza is killing more young and middle-aged adults this year than usual, in part because they're less likely to be vaccinated, federal health officials said Thursday.

More than 60 percent of those killed or put into the hospital by flu so far this season have been aged 18 to 64, the Centers for Disease Control and Prevention says. And 50 children [have died](#) of flu so far.

The good news is the vaccine is [pretty effective](#) for a flu vaccine, with a 61 percent effectiveness rate, CDC and other experts found.

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the **benefits** of **flu vaccination** 2015-2016

The estimated number of flu **illnesses prevented** by flu vaccination during the 2015-2016 season:

5 million

as many people use Denver International Airport in one month



The estimated number of flu **medical visits prevented** by vaccination during the 2015-2016 season:

2.5 million

equal to the population of Portland, Oregon



The estimated number of flu **hospitalizations prevented** by vaccination during the 2015-2016 season:

71,000

enough to fill every registered hospital bed in the state of Texas



DATA: Influenza Division program impact report 2015-2016, <https://www.cdc.gov/flu/about/diseases/2015-16.htm>.

NCIRDg-007 | 12/08/16



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

get **vaccinated**
www.cdc.gov/flu

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ACIP Says No to LAIV for 2017-18 Flu Season

Group Updates Influenza Vaccine Recommendations for Pregnant Women

June 30, 2017 07:35 am [Chris Crawford](#) – Just as it did for the 2016-2017 influenza season, the CDC's Advisory Committee on Immunization Practices (ACIP) has again decided to recommend against use of live attenuated influenza vaccine (LAIV; FluMist) for the 2017-2018 flu season because of the vaccine's reduced efficacy. This decision was made during the [ACIP's June 21-22 meeting](#). (www.cdc.gov)

Data presented at the meeting showed that last year's exclusion of LAIV didn't affect vaccine coverage numbers for the 2016-2017 season compared with the previous season, with the flu vaccine shown to be 42 percent effective in preventing infection from A and B viruses in patients of all ages.

For 2016-2017, influenza A accounted for 70 percent of circulating flu strains, with influenza B making up the other



Live Chat 

ORIGINAL ARTICLE

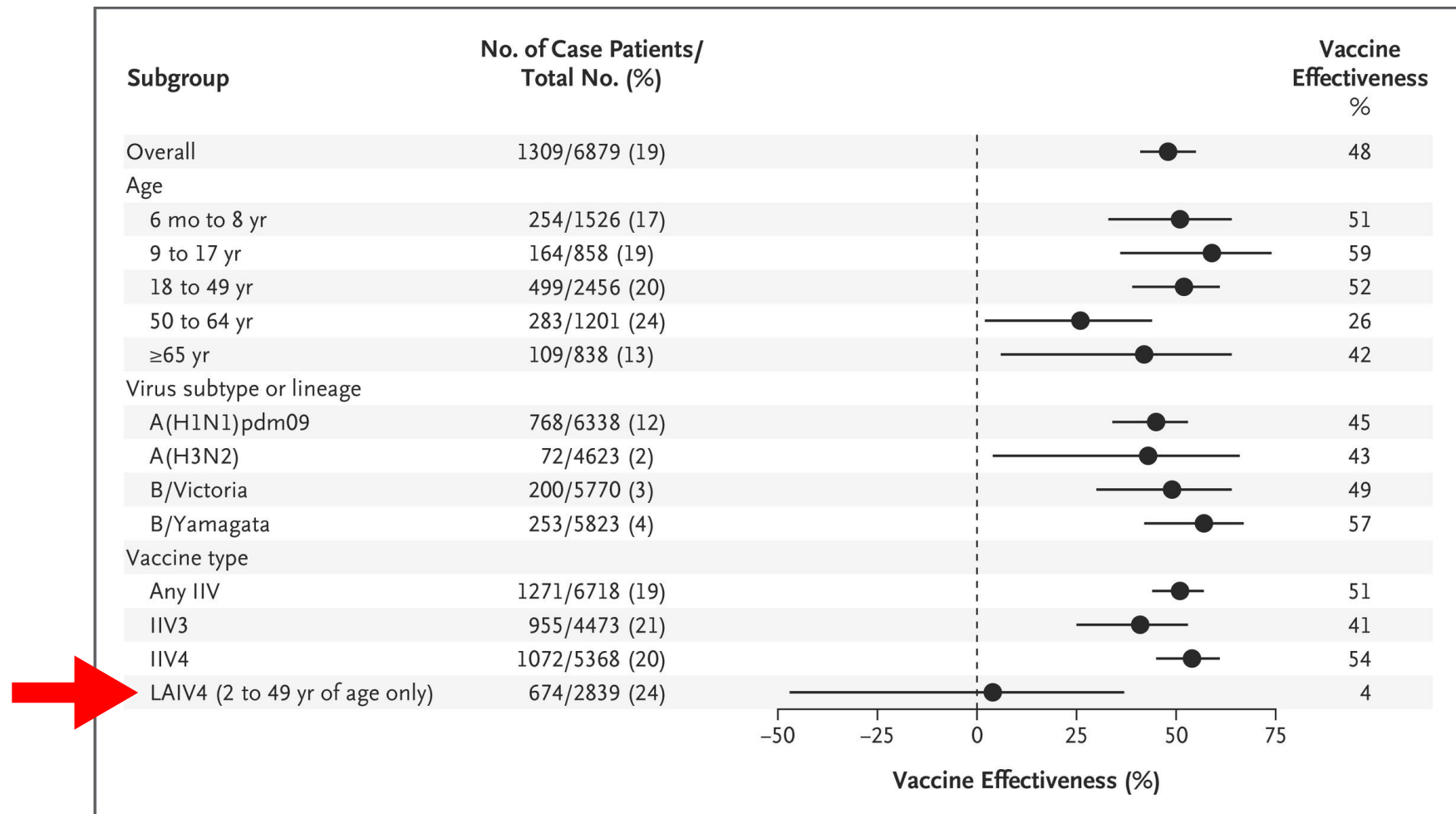
Influenza Vaccine Effectiveness in the United States during the 2015–2016 Season

Michael L. Jackson, Ph.D., Jessie R. Chung, M.P.H., Lisa A. Jackson, M.D.,
C. Hallie Phillips, M.Ed., Joyce Benoit, B.S.N., Arnold S. Monto, M.D.,
Emily T. Martin, Ph.D., Edward A. Belongia, M.D., Huong Q. McLean, Ph.D.,
Manjusha Gaglani, M.D., Kempapura Murthy, M.P.H., Richard Zimmerman, M.D.,
Mary P. Nowalk, Ph.D., Alicia M. Fry, M.D., and Brendan Flannery, Ph.D.


ABSTRACT

BACKGROUND

The A(H1N1)pdm09 virus strain used in the live attenuated influenza vaccine was changed for the 2015–2016 influenza season because of its lack of effectiveness in young children in 2013–2014. The Influenza Vaccine Effectiveness Network evaluated the effect of this change as part of its estimates of influenza vaccine effectiveness in 2015–2016.



SNP-mediated disruption of CTCF binding at the *IFITM3* promoter is associated with risk of severe influenza in humans

E Kaitlynn Allen¹, Adrienne G Randolph², Tushar Bhangale³, Pranay Dogra¹, Maikke Ohlson⁴, Christine M Oshansky^{1,9}, Anthony E Zamora¹, John P Shannon¹, David Finkelstein⁵, Amy Dressen³, John DeVincenzo^{6,7}, Miguela Caniza⁸, Ben Youngblood¹, Carrie M Rosenberger⁴ & Paul G Thomas¹ 

Previous studies have reported associations of *IFITM3* SNP rs12252 with severe influenza, but evidence of association and the mechanism by which risk is conferred remain controversial. We prioritized SNPs in *IFITM3* on the basis of putative biological function and identified rs34481144 in the 5' UTR. We found evidence of a new association of rs34481144 with severe influenza in three influenza-infected cohorts characterized by different levels of influenza illness severity. We determined a role for rs34481144 as an expression quantitative trait locus (eQTL) for *IFITM3*, with the risk allele associated with lower mRNA expression. The risk allele was found to have decreased IRF3 binding and increased CTCF binding in promoter-binding assays, and risk allele carriage diminished transcriptional correlations among *IFITM3*-neighboring genes, indicative of CTCF boundary activity. Furthermore, the risk allele disrupts a CpG site that undergoes differential methylation in CD8⁺ T cell subsets. Carriers of the risk allele had reduced numbers of CD8⁺ T cells in their airways during natural influenza infection, consistent with *IFITM3* promoting accumulation of CD8⁺ T cells in airways and indicating that a critical function for *IFITM3* may be to promote immune cell persistence at mucosal sites. Our study identifies a new regulator of *IFITM3* expression that associates with CD8⁺ T cell levels in the airways and a spectrum of clinical outcomes.

What is a medical device (as per FDA)?

“an instrument, apparatus...intended for use in the diagnosis of disease or other conditions...”

Can range from dental floss to prosthetic heart valve

https://commons.wikimedia.org/wiki/File:Aortic_Karboniks-1_bileafter_prosthetic_heart_valve.jpg

http://www.mwdental.com/media/catalog/product/cache/1/thumbnail/1000x1000/9df78eab33525d08d6e5fb8d27136e95/4/4/440-0500_6.jpg

FDA classification of a medical device:

- Based on the risks associated with the device
- One of three categories—Class I, Class II, and Class III

Class I devices

are deemed to be low risk and are therefore subject to the least regulatory controls (general controls).
e.g., dental floss

Class II devices

are higher risk devices than Class I and require greater regulatory controls to provide reasonable assurance of the device's safety and effectiveness (general and special controls).
e.g., powered wheel chairs

Class III devices

are generally the highest risk devices and are therefore subject to the highest level of regulatory control. Class III devices must typically be approved by FDA before they are marketed (pre-market approval).
e.g., replacement heart valves

General vs. special controls

- **General controls apply to all medical devices (unless exempt)**
 - Sufficient for low risk (Class I) devices
 - Include protections regulating adulteration/misbranding, registration, listing with FDA, Good Manufacturing Practices, proper labeling, and reporting adverse reactions, etc.
- **Special Controls are required when general controls alone are not sufficient (Class II)**
 - Include guidelines, performance standards, special labeling, etc.

What changed with rapid influenza virus antigen detection tests (RIDTs)?



- **These tests were classified as Class I devices**
 - General controls were considered sufficient
- **FDA has re-classified them to Class II**
 - Both general and special controls must now be followed

FDA decision

The screenshot displays the Federal Register website interface. At the top, there is a navigation bar with links for Sections, Browse, Search, Reader Aids, and My FR. A search bar is also present. Below the navigation bar is the Federal Register logo and the text "The Daily Journal of the United States Government". A blue banner across the page contains the word "Rule". The main heading of the document is "Microbiology Devices; Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly With Clinical Specimens". Below this, it states "A Rule by the Food and Drug Administration on 01/12/2017". The document is categorized as a "PUBLISHED DOCUMENT". On the left side, there is a sidebar with icons for a menu, comments (13), and document actions. The main content area is divided into sections: "AGENCY:" (Food and Drug Administration, HHS.), "ACTION:" (Final order.), and "SUMMARY:" (The Food and Drug Administration (FDA) is reclassifying antigen based rapid influenza virus antigen detection test systems intended to detect influenza virus directly from clinical specimens that are currently regulated as influenza virus serological reagents from class I into class II with special controls and into a new device classification regulation.). On the right side, there is a "DOCUMENT DETAILS" section with the following information: "Printed version: PDF", "Publication Date: 01/12/2017", "Agencies: Food and Drug Administration", "Dates: This order is effective February 13, 2017. See further discussion in section IV, 'Implementation Strategy.'", "Effective Date: 02/13/2017", "Document Type: Rule", and "Document Citation:". A "Site Feedback" link is located in the top right corner.

FEDERAL REGISTER
The Daily Journal of the United States Government

Microbiology Devices; Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly With Clinical Specimens

A Rule by the Food and Drug Administration on 01/12/2017

PUBLISHED DOCUMENT

AGENCY:
Food and Drug Administration, HHS.

ACTION:
Final order.

SUMMARY:
The Food and Drug Administration (FDA) is reclassifying antigen based rapid influenza virus antigen detection test systems intended to detect influenza virus directly from clinical specimens that are currently regulated as influenza virus serological reagents from class I into class II with special controls and into a new device classification regulation.

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Document Citation:

Why the change with RIDTs?

- During the H1N1 influenza pandemic of 2009, questions were raised about the sensitivity of RIDTs
 - Lower sensitivity than package insert
- Concerns raised about the overall quality of influenza testing
- **Overall goal:** lower the number of misdiagnosed influenza infections by increasing the number of devices that can reliably detect the influenza virus

Why have rapid antigen tests been re-classified?

“A false negative result may lead to failure to provide a correct diagnosis and the appropriate treatment of infection caused by influenza virus and may contribute to unnecessary treatment for another suspected condition. A false negative result will also provide incorrect epidemiological information leading to failure to initiate appropriate corrective measures to control and prevent additional infections.”

“A false positive result on the other hand may lead to delayed treatment of a respiratory infection caused by another etiologic agent, which could potentially result in a more serious patient outcome. A false positive result will also provide incorrect epidemiological information on the presence of influenza in a community, which may result in unnecessary patient isolation or contact limitations and in unnecessary close contact investigations.”

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/UCM356185.pdf>

Minimum acceptance criteria

Sensitivity

Flu A Point estimate of 90% with 80% lower bound of the 95% confidence interval

Flu B Point estimate of 80% with 70% lower bound of the 95% confidence interval

Specificity

All influenza detection devices should demonstrate specificity with a lower bound of the 95% confidence interval exceeding 90% for both, Flu A and Flu B.

b. When compared to a molecular comparator method:

Sensitivity

Flu A Point estimate of 80% with 70% lower bound of the 95% confidence interval

Flu B Point estimate of 80% with 70% lower bound of the 95% confidence interval

Specificity

All influenza detection devices should demonstrate a specificity estimate with a lower bound of the 95% confidence interval exceeding 90% for both, influenza A and influenza B.

21 CFR Part 866

The screenshot displays the GPO's Federal Digital System (FDsys) interface. The top navigation bar includes links for About GPO, Newsroom/Media, Congressional Relations, Inspector General, Careers, Contact, askGPO, and Help. The main header features the GPO logo and the text "U.S. GOVERNMENT PUBLISHING OFFICE | Keeping America Informed". Below this, a secondary navigation bar lists Home, Customers, Vendors, and Libraries.

On the left side, the "FDsys:" section provides links to "GPO's Federal Digital System", "About FDsys", "Search Government Publications", and "Browse Government Publications". A "Browse / Search Previous" button is also present. A list of search options includes "Browse", "Simple Search", "Advanced Search", "Boolean", "Proximity", "Search History", "Search Tips", "Corrections", "Latest Updates", "User Info", "FAQs", "Agency List", and "Incorporation By Reference". A "Related Resources" section at the bottom left lists "The Code of Federal Regulations (CFR)" and "e-CFR".

The main content area is titled "ELECTRONIC CODE OF FEDERAL REGULATIONS". It features a box with the text "View past updates to the e-CFR. Click here to learn more." and a red banner stating "e-CFR data is current as of September 21, 2017". Below this, a breadcrumb trail shows "Title 21 → Chapter I → Subchapter H → Part 866". Links for "Browse Previous" and "Browse Next" are provided. The current section is "Title 21: Food and Drugs".

The "PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES" section is highlighted with a red arrow. It includes a "Contents" table of contents with the following entries:


Subpart A—General Provisions	
§866.1	Scope.
§866.3	Effective dates of requirement for premarket approval.
§866.9	Limitations of exemptions from section 510(k) of the Federal Food, Drug, and Cosmetic Act (the act).

Subpart B—Diagnostic Devices	
§866.1620	Antimicrobial susceptibility test disc.
§866.1640	Antimicrobial susceptibility test powder.
§866.1645	Fully automated short-term incubation cycle antimicrobial susceptibility system.
§866.1700	Culture medium for antimicrobial susceptibility tests.

21 CFR Part 866

[47 FR 50823, Nov. 9, 1982, as amended at 63 FR 59227, Nov. 3, 1998]

 [Back to Top](#)



§866.3328 Influenza virus antigen detection test system.

(a) *Identification.* An influenza virus antigen detection test system is a device intended for the qualitative detection of influenza viral antigens directly from clinical specimens in patients with signs and symptoms of respiratory infection. The test aids in the diagnosis of influenza infection and provides epidemiological information on influenza. Due to the propensity of the virus to mutate, new strains emerge over time which may potentially affect the performance of these devices. Because influenza is highly contagious and may lead to an acute respiratory tract infection causing severe illness and even death, the accuracy of these devices has serious public health implications.

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) The device's sensitivity and specificity performance characteristics or positive percent agreement and negative percent agreement, for each specimen type claimed in the intended use of the device, must meet one of the following two minimum clinical performance criteria:

(i) For devices evaluated as compared to an FDA-cleared nucleic acid based-test or other currently appropriate and FDA accepted comparator method other than correctly performed viral culture method:

(A) The positive percent agreement estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 80 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 70 percent.

(B) The negative percent agreement estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 95 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 90 percent.

(ii) For devices evaluated as compared to correctly performed viral culture method as the comparator method:

(A) The sensitivity estimate for the device when testing for influenza A must be at the point estimate of at least 90 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 80 percent. The sensitivity estimate for the device when testing for influenza B must be at the point estimate of at least 80 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 70 percent.

(B) The specificity estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 95 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 90 percent.

(2) When performing testing to demonstrate the device meets the requirements in paragraph (b)(1) of this section, a currently appropriate and FDA accepted comparator method must be used to establish assay performance in clinical studies.

(3) Annual analytical reactivity testing of the device must be performed with contemporary influenza strains. This annual analytical reactivity testing must meet the following criteria:

(i) The appropriate strains to be tested will be identified by FDA in consultation with the Centers for Disease Control and Prevention (CDC) and sourced from CDC or an FDA-designated source. If the annual strains are not available from

What is the timeline for this change?

- Rule was published 01/12/2017
 - Effective Date: 02/13/2017
- For antigen-based RIDTs legally marketed prior to 2/13/2017:
 - Manufacturers must obtain a new 510(k) clearance and demonstrate compliance with the special controls included in the new clinical performance standards before marketing their changed or new devices
- FDA will allow for a one year transition before enforcement of new rule (January 12, 2018)

Enforcing compliance



“For antigen based RIDTs that have been legally marketed prior to February 13, 2017, FDA does not intend to enforce compliance with the special controls until January 12, 2018. If a manufacturer markets such a device after January 12, 2018, and that device does not comply with the special controls, then FDA would consider taking action against such a manufacturer under its usual enforcement policies.”

What does this change mean for you?

- Tests that are not compliant with new regulations can be purchased up until January 12th, 2018.
 - Cannot be sold by manufacturers or distributors after this date
- Purchased tests can be used by customers until their expiration date.
 - Using these kits is NOT a violation
 - No changes for the 2018 flu season are necessary if enough kits are purchased for the duration of the season before 1/12/2018
- Clinics should begin to look into new assays that are compliant with new regulations with next season in mind.

CLIA regulations for testing



- All laboratory testing in the U.S. falls under the jurisdiction of Clinical Laboratory Improvement Amendments of 1988 (CLIA)
- Administered by CMS and is implemented through three federal agencies—CDC, CMS, and the Food and Drug Administration (FDA)
- The three categories of testing for CLIA purposes are **waived, moderate complexity** (including the provider-performed microscopy procedures [PPMP] subcategory), and **high complexity**

CLIA regulations for testing



- Waived, moderate complexity, and high complexity designation based on ease of use
- CLIA requires that waived tests must be simple and have a low risk for erroneous results
- Tests classified as moderately complex must be performed in a clinical laboratory

Influenza testing methodologies

Method ¹	Types Detected	Acceptable Specimens ²	Test Time	CLIA Waived ³
Rapid Influenza Diagnostic Tests ⁴ (antigen detection)	A and B	NP ⁵ swab, aspirate or wash, nasal swab, aspirate or wash, throat swab	<15 min.	Yes/No
Rapid Molecular Assay [influenza viral RNA or nucleic acid detection]	A and B	NP ⁵ swab, nasal swab	<20 minutes ⁶	Yes/No ⁶
Immunofluorescence, Direct (DFA) or Indirect (IFA) Florescent Antibody Staining [antigen detection]	A and B	NP ⁴ swab or wash, bronchial wash, nasal or endotracheal aspirate	1-4 hours	No
RT-PCR ⁷ (singleplex and multiplex; real-time and other RNA-based) and other molecular assays [influenza viral RNA or nucleic acid detection]	A and B	NP ⁵ swab, throat swab, NP ⁵ or bronchial wash, nasal or endotracheal aspirate, sputum	Varies (1 to 8 hours, varies by the assay)	No
Rapid cell culture (shell vials; cell mixtures; yields live virus)	A and B	NP ⁵ swab, throat swab, NP ⁵ or bronchial wash, nasal or endotracheal aspirate, sputum; (specimens placed in VTM ⁸)	1-3 days	No
Viral tissue cell culture (conventional; yields live virus)	A and B	NP ⁵ swab, throat swab, NP ⁵ or bronchial wash, nasal or endotracheal aspirate, sputum (specimens placed in VTM)		

CDC. Rapid Diagnostic Testing for Influenza: Information for Clinical Laboratory Directors
<https://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm#table2>

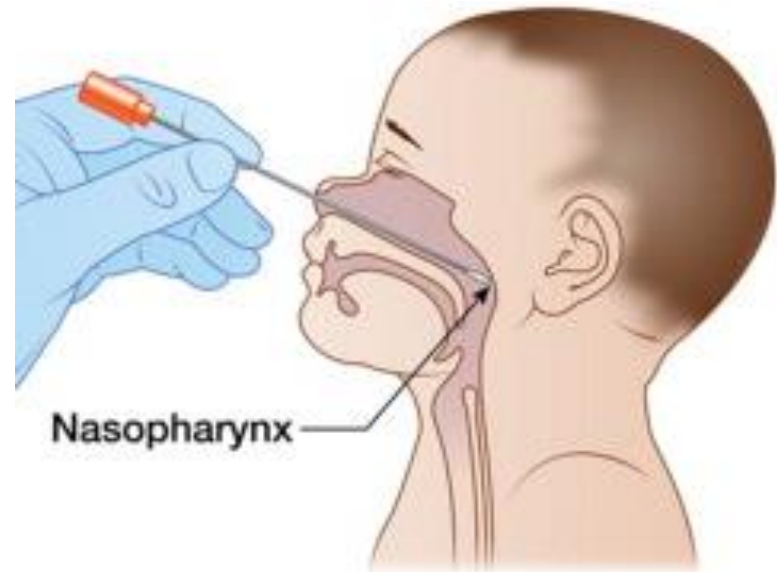
Point-of-care testing (POCT)



- These are CLIA waived tests that can be performed by facilities with a Certificate of Waiver
- Increasingly larger portion of patient testing
- Huge advantage of rapid answer for treatment decisions
- QUALITY is key

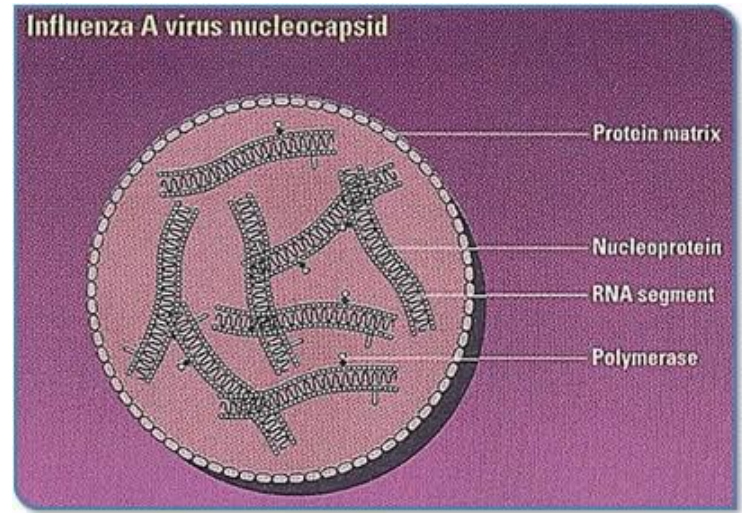
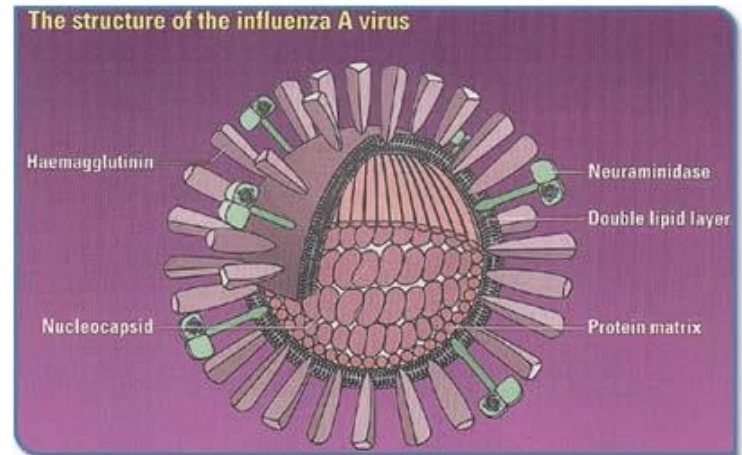
Specimen collection

- Ideally, collected within 3 days of symptom onset.
1. Use sterile Dacron/nylon swab.
 2. Insert into the posterior pharynx and tonsillar areas.
 3. Remove swab and place into viral transport medium.
 4. Test ASAP or keep specimen at 4°C.



RIDTs targets

- Immunoassays—identify influenza A&B viral nucleoprotein antigens
- The nucleoproteins are conserved throughout a given species
- Qualitative resulting



RIDTs pros and cons

Pros

- Rapid results
- Simple to use
- Several designated as CLIA waived (POCT eligible)

Cons

- Poor sensitivity
 - False negatives common
- Bad at detecting novel viral strains



CLIA waived RIDTs options

BD Veritor™ System for Rapid Detection of Flu A+B



Chromatographic immunoassay with automated reader design

- **Run time:** 10 minutes
- **Specimen types:** Direct Nasal and Nasopharyngeal swabs **Moderately complex liquid nasopharyngeal wash, aspirate and swab in transport media samples*

Alere™ Influenza A&B Test



Dipstick design with visual read

- **Run time:** 10 minutes
- **Specimen types:** Nasal swab specimens

Meridian ImmunocardSTAT®! Flu A&B

Dipstick design with visual read

- **Run time:** 10 - 15 minutes
- **Specimen types:** Nasal and nasal pharyngeal swab specimens **Moderate Complexity when used with Nasal Wash/Aspirate Samples*

Sekisui OSOM® Ultra Influenza A & B



Immunochromatographic assay with visual read

- **Run time:** 10 – 15 minutes
- **Specimen types:** Nasal and nasopharyngeal swab **Moderately complex nasal aspirate/wash specimens*

LifeSign Status Flu A & B

In vitro rapid qualitative test – lateral flow

- **Run time:** 10 minutes
- **Specimen types:** Nasal swab, nasopharyngeal swab **Moderately complex nasal aspirate/wash specimens*

Quidel Sofia® Analyzer and Influenza A+B FIA



Lateral flow immunoassay+ fluorescence
with automated reader

- **Run time:** 15 minutes
- **Specimen types:** Direct Nasal swab, nasopharyngeal swab and nasopharyngeal aspirate/wash specimens

Molecular tests for flu

- Traditionally designated by CLIA as moderate/high complexity and have been performed in the clinical laboratories
 - Only rapid antigen influenza testing was available as CLIA waived
- CLIA waived tests for influenza have become available in the past two years

CLIA waived molecular tests for flu



- **January 8th, 2015:** First CLIA waived test for influenza A and B (Alere i Influenza A&B)
- Followed by the Roche cobas[®] LIAT Influenza A/B
- Both of these tests are classified as class II, so they are already compliant

Molecular flu testing pros and cons

Pros

- Can amplify genome
- Highly sensitive and specific

Cons

- Typically costs more
- Takes longer



CLIA waived molecular influenza testing options

Alere™ i Influenza A&B



- FDA-cleared for use with both nasal swabs (direct) and NP or nasal swabs in VTM
 - CLIA-waived for use with nasal swabs (direct) only
- < 15 minutes to results
- Footprint: 8.15"W x 5.71"H x 7.64"D
- 1.4 lbs / 3 kg

Roche cobas[®] LIAT Influenza A/B



- CLIA-waived by FDA for use with nasopharyngeal swabs only
- 20 minutes to results
- Footprint: 4.5"W x 9.5"H x 7.5"D
- Weight 8.3 lbs

Review: tests that are (or will be) compliant



- Any test already classified as a Class II device:
 - Rapid molecular influenza tests
- Certain RIDTs that have already met, or applied for and were granted Class II status
- Any test that obtains a new 510(k) clearance to be Class II

Influenza testing platforms that meet reclassification*



Product name	Product type	CLIA	Complexity
Alere/Alere I	Molecular	Waived	Low
Roche cobas [®] Liat	Molecular	Waived	Low
Quidel Solana	Molecular	Non-Waived	Moderate
BD Veritor	Reader	Waived (Physician) Non-Waived (Laboratory)	Low Moderate
Quidel Sofia1 & Sofia2	Reader	Waived	Low
Alere Dipstick Flu A&B	Visual	Waived	Low
LifeSign Status Flu A&B	Visual	Waived	Low
Meridian Immunocard STAT [®] ! Flu A&B	Visual	Waived	Low
Remel Xpect [™] Flu A&B	Visual	Non-Waived	Moderate
Sekisui Osom [®] Ultra Flu A&B	Visual	Waived	Low

*Current as of September 2017

Summary



- RIDTs that are currently classified as I will no longer be sold after January 12th, 2018
- Tests purchased before January 12th, 2018 can be used by customers until their expiration date
- There are several tests already on the market (both rapid antigen and molecular options) that are already compliant with new regulations

Speak with your distributor and influenza test manufacturer to ensure you are prepared for the influenza season.

Questions?

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The information in this presentation is provided for educational purposes only and is not legal advice. It is intended to highlight laws you are likely to encounter, but is not a comprehensive review. If you have questions or concerns about a particular instance or whether a law applies, you should consider contacting your attorney.



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